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(FILE 'HOME' ENTERED AT 13:33:24 ON 09 JAN 2002)

FILE 'USPATFULL' ENTERED AT 13:40:16 ON 09 JAN 2002

L1 5 S ((SHARK CARTILAGE) (2A) EXTRACT)/CLM  
L2 1 S ((SHARK CARTILAGE) (2A) EXTRACT) AND (ANTI(W)HYPERTENS? OR AN  
L3 2 S (SHARK CARTILAGE) AND (ANTI(W)HYPERTENS? OR ANTIHYPERTENSIVE  
L4 1 S L3 NOT L2

FILE 'CAPLUS' ENTERED AT 13:54:01 ON 09 JAN 2002

L5 1 S L2

FILE 'WPIDS' ENTERED AT 13:55:00 ON 09 JAN 2002

L6 1 S L2  
L7 5 S (ANTI(2W)ANGIOGENES?) AND (ANTI(W)HYPERTENS? OR ANTIHYPERTENS

FILE 'CAPLUS' ENTERED AT 14:06:52 ON 09 JAN 2002

L8 2 S (ANTI(2W)ANGIOGENES?) AND (ANTI(W)HYPERTENS? OR ANTIHYPERTENS

FILE 'USPATFULL' ENTERED AT 14:07:50 ON 09 JAN 2002

L9 0 S ((ANTI(2W)ANGIOGENES?) AND (ANTI(W)HYPERTENS? OR ANTIHYPERTEN  
L10 12 S ((ANTI(2W)ANGIOGENES?) AND (ANTI(W)HYPERTENS? OR ANTIHYPERTEN

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NEWS	3	Feb 06	Engineering Information Encompass files have new names
NEWS	4	Feb 16	TOXLINE no longer being updated
NEWS	5	Apr 23	Search Derwent WPINDEX by chemical structure
NEWS	6	Apr 23	PRE-1967 REFERENCES NOW SEARCHABLE IN CAPLUS AND CA
NEWS	7	May 07	DGENE Reload
NEWS	8	Jun 20	Published patent applications (A1) are now in USPATFULL
NEWS	9	JUL 13	New SDI alert frequency now available in Derwent's DWPI and DPCI
NEWS	10	Aug 23	In-process records and more frequent updates now in MEDLINE
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NEWS	14	Oct 09	Korean abstracts now included in Derwent World Patents Index
NEWS	15	Oct 09	Number of Derwent World Patents Index updates increased
NEWS	16	Oct 15	Calculated properties now in the REGISTRY/ZREGISTRY File
NEWS	17	Oct 22	Over 1 million reactions added to CASREACT
NEWS	18	Oct 22	DGENE GETSIM has been improved
NEWS	19	Oct 29	AAASD no longer available
NEWS	20	Nov 19	New Search Capabilities USPATFULL and USPAT2
NEWS	21	Nov 19	TOXCENTER(SM) - new toxicology file now available on STN
NEWS	22	Nov 29	COPPERLIT now available on STN
NEWS	23	Nov 29	DWPI revisions to NTIS and US Provisional Numbers
NEWS	24	Nov 30	Files VETU and VETB to have open access
NEWS	25	Dec 10	WPINDEX/WPIDS/WPIX New and Revised Manual Codes for 2002
NEWS	26	Dec 10	DGENE BLAST Homology Search
NEWS	27	Dec 17	WELDASEARCH now available on STN
NEWS	28	Dec 17	STANDARDS now available on STN
NEWS	29	Dec 17	New fields for DPCI
NEWS	30	Dec 19	CAS Roles modified
NEWS	31	Dec 19	1907-1946 data and page images added to CA and Caplus
NEWS EXPRESS			August 15 CURRENT WINDOWS VERSION IS V6.0c, CURRENT MACINTOSH VERSION IS V6.0 (ENG) AND V6.0J (JP), AND CURRENT DISCOVER FILE IS DATED 07 AUGUST 2001
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FILE 'HOME' ENTERED AT 13:33:24 ON 09 JAN 2002

=> file uspatfull

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

1.80

1.80

FILE 'USPATFULL' ENTERED AT 13:40:16 ON 09 JAN 2002

CA INDEXING COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 8 Jan 2002 (20020108/PD)

FILE LAST UPDATED: 8 Jan 2002 (20020108/ED)

HIGHEST GRANTED PATENT NUMBER: US6338160

HIGHEST APPLICATION PUBLICATION NUMBER: US2001047529

CA INDEXING IS CURRENT THROUGH 8 Jan 2002 (20020108/UPCA)

ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 8 Jan 2002 (20020108/PD)

REVISED CLASS FIELDS (/NCL) LAST RELOADED: Oct 2001

USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Oct 2001

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>>> USPAT2 is now available. USPATFULL contains full text of the <<<
>>> original, i.e., the earliest published granted patents or <<<
>>> applications. USPAT2 contains full text of the latest US <<<
>>> publications, starting in 2001, for the inventions covered in <<<
>>> USPATFULL. A USPATFULL record contains not only the original <<<
>>> published document but also a list of any subsequent <<<
>>> publications. The publication number, patent kind code, and <<<
>>> publication date for all the US publications for an invention <<<
>>> are displayed in the PI (Patent Information) field of USPATFULL <<<
>>> records and may be searched in standard search fields, e.g., /PN, <<<
>>> /PK, etc. <<<
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>>> USPATFULL and USPAT2 can be accessed and searched together <<<
>>> through the new cluster USPATALL. Type FILE USPATALL to <<<
>>> enter this cluster. <<<
>>> <<<
>>> Use USPATALL when searching terms such as patent assignees, <<<
>>> classifications, or claims, that may potentially change from <<<
>>> the earliest to the latest publication. <<<
```

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s ((shark cartilage) (2a) extract)/clm

164 SHARK/CLM

24 SHARKS/CLM

177 SHARK/CLM

((SHARK OR SHARKS)/CLM)

700 CARTILAGE/CLM

24 CARTILAGES/CLM

715 CARTILAGE/CLM

((CARTILAGE OR CARTILAGES)/CLM)

14 SHARK CARTILAGE/CLM

((SHARK(W) CARTILAGE)/CLM)

14613 EXTRACT/CLM

3768 EXTRACTS/CLM

17451 EXTRACT/CLM

((EXTRACT OR EXTRACTS)/CLM)

L1 5 ((SHARK CARTILAGE) (2A) EXTRACT)/CLM

=> d bib,kwic 1-5

L1 ANSWER 1 OF 5 USPATFULL

AN 2000:21612 USPATFULL

TI Methods of using extracts of shark cartilage

IN Dupont, Eric, St. Nicholas, Canada

Brazeau, Paul, Montreal, Canada

Juneau, Christina, Ste. Foy, Canada

Maes, Daniel H., Huntington, NY, United States

Mareus, Kenneth, Dix Hills, NY, United States

PA Les Laboratoires Aeterna Inc., Quebec, Canada (non-U.S. corporation)

PI US 6028118 20000222

AI US 1996-693535 19960808 (8)

DT Utility

FS Granted

EXNAM Primary Examiner: Eisenschenk, Frank C.; Assistant Examiner: Nelson, Brett

LREP Matos, RickAkin, Gump, Strauss, Hauer & Feld, L.L.P.

CLMN Number of Claims: 12

ECL Exemplary Claim: 1

DRWN 31 Drawing Figure(s); 26 Drawing Page(s)

LN.CNT 2317

CLM What is claimed is:

- . . . to transepidermal water loss, said method comprising the step of applying to the skin a therapeutically effective amount of a **shark cartilage extract** obtained by a process comprising the steps of: a) homogenizing shark cartilage in an aqueous solution in conditions which are. . .
- . . . soothing irritated mammalian skin, said method comprising the step of applying to the skin a therapeutically effective amount of a **shark cartilage extract** obtained by a process comprising the steps of: a) homogenizing shark cartilage in an aqueous solution in conditions which are. . .
- . . . inflammation in mammalian skin, said method comprising the step of applying to the skin a therapeutically effective amount of a **shark cartilage extract** obtained by a process comprising the steps of: a) homogenizing shark cartilage in an aqueous solution in conditions which are. . .
- . . . activity in mammalian skin, said method comprising the step of applying to the skin a therapeutically effective amount of a **shark cartilage extract** obtained by a process comprising the steps of: a) homogenizing shark cartilage in an aqueous solution in conditions which are. . .
- . . . atrophy in mammalian skin, said method comprising the step of applying to the skin a therapeutically effective amount of a **shark cartilage extract** obtained by a process comprising the steps of: a) homogenizing shark cartilage in an aqueous solution in conditions which are. . .
- . . . acne in mammalian skin, said method comprising the step of applying to the skin a therapeutically effective amount of a **shark cartilage extract** obtained by a process comprising the steps of: a) homogenizing shark cartilage in an aqueous solution in conditions which are. . .
- . . . psoriasis in mammalian skin, said method comprising the step of applying to the skin a therapeutically effective amount of a **shark cartilage extract** obtained by a process comprising the steps of: a) homogenizing shark cartilage in an aqueous solution in conditions which are. . .

- . . . aging in mammalian skin, said method comprising the step of applying to the skin a therapeutically effective amount of a **shark cartilage extract** obtained by a process comprising the steps of: a) homogenizing shark cartilage in an aqueous solution in conditions which are. . .
- . . . eczema in mammalian skin, said method comprising the step of applying to the skin a therapeutically effective amount of a **shark cartilage extract** obtained by a process comprising the steps of: a) homogenizing shark cartilage in an aqueous solution in conditions which are. . .

L1 ANSWER 2 OF 5 USPATFULL

AN 2000:18419 USPATFULL

TI Extracts of shark cartilage having anti-collagenolytic, anti-inflammatory, anti-angiogenic and anti-tumoral activities; process of making, methods of using and compositions thereof

IN Dupont, Eric, St. Nicolas, Canada

Brazeau, Paul, Montreal, Canada

Juneau, Christina, Ste. Foy, Canada

Maes, Daniel H., Huntington, NY, United States

Marens, Kenneth, Dix Hills, NY, United States

PA Les Laboratoires Aeterna Inc., Canada (non-U.S. corporation)

PI US 6025334 20000215

AI US 1995-550003 19951030 (8)

RLI Continuation-in-part of Ser. No. US 1995-384555, filed on 3 Feb 1995, now patented, Pat. No. US 5618925, issued on 8 Apr 1997 which is a continuation-in-part of Ser. No. US 1994-234019, filed on 28 Apr 1994, now abandoned

DT Utility

FS Granted

EXNAM Primary Examiner: Tsang, Cecilia J.; Assistant Examiner: Mohamed, Abdel A.

LREP Matos, RickAkin, Gump, Strauss, Hauer & Feld, L.L.P.

CLMN Number of Claims: 28

ECL Exemplary Claim: 1

DRWN 31 Drawing Figure(s); 17 Drawing Page(s)

LN.CNT 1732

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

CLM What is claimed is:

- . . . of tumor proliferation, angiogenesis, inflammation and collagenolysis, the topical formulation comprising a pharmaceutical composition comprising an effective amount of a **shark cartilage extract** and an antioxidant, said **shark cartilage extract** being prepared according to a process comprising the steps of: a) homogenizing the cartilage in an aqueous solution in conditions. . .
- . . . the method comprising the step of administering to a patient in need of such treatment an effective amount of a **shark cartilage extract**, said **shark cartilage extract** being prepared according to a process which comprises the following steps: a) homogenizing the cartilage in an aqueous solution in. . .

L1 ANSWER 3 OF 5 USPATFULL

AN 1999:146538 USPATFULL

TI Extracts of shark cartilage having an anti-angiogenic activity and an effect on tumor regression: process of making thereof

IN Dupont, Eric, St. Nicolas, Canada

Brazeau, Paul, Montreal, Canada

Juneau, Christian, Ste. Foy, Canada

PA Les Laboratoires Aeterna Inc., Quebec, Canada (non-U.S. corporation)

PI US 5985839 19991116

AI US 1996-727300 19961008 (8)  
RLI Continuation of Ser. No. US 1995-384555, filed on 3 Feb 1995, now  
patented, Pat. No. US 5618925 which is a continuation-in-part of Ser.  
No. US 1994-234019, filed on 28 Apr 1994, now abandoned  
DT Utility  
FS Granted  
EXNAM Primary Examiner: Tsang, Cecilia; Assistant Examiner: Mohamed, Abdel A.  
LREP Matos, RickAkin, Gump, Strauss, Hauer & Feld, L.L.P.  
CLMN Number of Claims: 57  
ECL Exemplary Claim: 1  
DRWN 7 Drawing Figure(s); 14 Drawing Page(s)  
LN.CNT 1282

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

CLM What is claimed is:

51. A **shark cartilage extract** comprising  
at least one biologically active component having a molecular weight of  
less than about 500 KDa; an anti-angiogenic activity;. . .
52. A **shark cartilage extract** according to  
claim 51, wherein said at least one biologically active component has a  
molecular weight in the range of. . .
53. A **shark cartilage extract** according to  
claim 51, wherein said at least one biologically active component  
comprises at least one biologically active component having. . .
54. A **shark cartilage extract** according to  
claim 51, wherein said at least at one biologically active component  
comprises at least one biologically active component. . .
55. A pharmaceutical composition comprising a **shark  
cartilage extract** as defined in claim 51.

. . . said method comprising the step of administering to a patient in need  
of such treatment an effective amount of a **shark  
cartilage extract** as defined in claim 51 for a period  
of time to sufficient treat said diseases or disorders.

L1 ANSWER 4 OF 5 USPATFULL  
AN 97:29579 USPATFULL  
TI Extracts of shark cartilage having an anti-angiogenic activity and an  
effect on tumor regression; process of making thereof  
IN Dupont, Eric, St. Nicolas, Canada  
Brazeau, Paul, Montreal, Canada  
Juneau, Christi, Ste. Foy, Canada  
PA Les Laboratories Aeterna Inc., Quebec, Canada (non-U.S. corporation)  
PI US 5618925 19970408  
AI US 1995-384555 19950203 (8)  
RLI Continuation-in-part of Ser. No. US 1994-234019, filed on 28 Apr 1994  
DT Utility  
FS Granted  
EXNAM Primary Examiner: Weimar, Elizabeth C.; Assistant Examiner: Mohamed,  
Abdel A.  
LREP Cushman Darby & Cushman IP Group of Pillsbury Madison & Sutro LLP  
CLMN Number of Claims: 28  
ECL Exemplary Claim: 1  
DRWN 16 Drawing Figure(s); 14 Drawing Page(s)  
LN.CNT 1153

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

CLM What is claimed is:

1. A process for obtaining a solid **extract** of **shark  
cartilage** having anti-angiogenic, direct anti-tumoral and  
anti-tumor proliferating activities, which comprises the following  
steps: a) homogenizing pieces of solid shark cartilage. . .
7. A process for obtaining a liquid **extract** of **shark**

**cartilage** which comprises the following steps: a) homogenizing pieces of solid shark cartilage in a non-denaturing aqueous solution until said pieces. . . .  
 26. A process for obtaining a liquid **extract** of **shark cartilage** having anti-angiogenic, direct anti-tumoral and anti-tumor proliferating activities which comprises the following steps, all performed at about 4.degree. C.: a). . . .

L1 ANSWER 5 OF 5 USPATFULL  
 AN 84:53979 USPATFULL  
 TI Anti-inflammatory composition  
 IN Schinitzky, Michael, Madison, WI, United States  
 PA Faxon Pharmaceuticals, Inc., Madison, WI, United States (U.S. corporation)  
 PI US 4473551 19840925  
 AI US 1983-502716 19830609 (6)  
 RLI Continuation-in-part of Ser. No. US 1982-410447, filed on 23 Aug 1982, now abandoned  
 DT Utility  
 FS Granted  
 EXNAM Primary Examiner: Rosen, Sam  
 LREP Barnes & Thornburg  
 CLMN Number of Claims: 21  
 ECL Exemplary Claim: 1  
 DRWN No Drawings  
 LN.CNT 344  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 CLM What is claimed is:  
 . . . 10 wherein said cartilage is administered in the form of the greater than 100,000 molecular weight fraction of an aqueous **extract** of whole **shark cartilage**.

=> d pn 1-5

L1 ANSWER 1 OF 5 USPATFULL  
 PI US 6028118 20000222  
  
 L1 ANSWER 2 OF 5 USPATFULL  
 PI US 6025334 20000215  
  
 L1 ANSWER 3 OF 5 USPATFULL  
 PI US 5985839 19991116  
  
 L1 ANSWER 4 OF 5 USPATFULL  
 PI US 5618925 19970408  
  
 L1 ANSWER 5 OF 5 USPATFULL  
 PI US 4473551 19840925

=> d ai 1-5

L1 ANSWER 1 OF 5 USPATFULL  
 AI US 1996-693535 19960808 (8)  
  
 L1 ANSWER 2 OF 5 USPATFULL  
 AI US 1995-550003 19951030 (8)  
  
 L1 ANSWER 3 OF 5 USPATFULL  
 AI US 1996-727300 19961008 (8)

L1 ANSWER 4 OF 5 USPATFULL  
AI US 1995-384555 19950203 (8)

L1 ANSWER 5 OF 5 USPATFULL  
AI US 1983-502716 19830609 (6)

=> s ((shark cartilage) (2a) extract) and (anti(w)hypertens? or antihypertensive or ((Calcium or Ca) (2w) blocker#) or verapamil or nifedipin or diltiasem)

1189 SHARK  
351 SHARKS  
1407 SHARK  
(SHARK OR SHARKS)  
6873 CARTILAGE  
447 CARTILAGES  
7064 CARTILAGE  
(CARTILAGE OR CARTILAGES)  
88 SHARK CARTILAGE  
(SHARK (W) CARTILAGE)  
143384 EXTRACT  
95409 EXTRACTS  
191564 EXTRACT  
(EXTRACT OR EXTRACTS)  
9 (SHARK CARTILAGE) (2A) EXTRACT  
220674 ANTI  
19 ANTIS  
220683 ANTI  
(ANTI OR ANTIS)  
16378 HYPERTENS?  
2456 ANTI (W) HYPERTENS?  
5646 ANTIHYPERTENSIVE  
1789 ANTIHYPERTENSIVES  
6689 ANTIHYPERTENSIVE  
(ANTIHYPERTENSIVE OR ANTIHYPERTENSIVES)  
215896 CALCIUM  
54 CALCIUMS  
215898 CALCIUM  
(CALCIUM OR CALCIUMS)  
111832 CA  
12083 CAS  
121951 CA  
(CA OR CAS)  
10010 BLOCKER#  
2056 (CALCIUM OR CA) (2W) BLOCKER#  
1928 VERAPAMIL  
3 VERAPAMILS  
1928 VERAPAMIL  
(VERAPAMIL OR VERAPAMILS)  
82 NIFEDIPIN  
2 DILTIASEM  
L2 1 ((SHARK CARTILAGE) (2A) EXTRACT) AND (ANTI (W) HYPERTENS? OR ANTIHYPERTENSIVE OR ((CALCIUM OR CA) (2W) BLOCKER#) OR VERAPAMIL OR NIFEDIPIN OR DILTIASEM)

=> d kwic

L2 ANSWER 1 OF 1 USPATFULL

DETD . . . compounds that interfere with DNA replication, mitosis and chromosomal segregation. Such chemotherapeutic compounds include adriamycin, also known as doxorubicin, etoposide, **verapamil**, podophyllotoxin, and the like. Widely used in a clinical setting for the



treatment of neoplasms, these compounds are administered through. . .

DETD CAI is a small molecular weight synthetic inhibitor of angiogenesis that acts as a **calcium channel blocker** that prevents actin reorganization, endothelial cell migration and spreading on collagen IV. CAI inhibits neovascularization at physiological attainable concentrations and. . .

DETD . . . acids and paclitaxel (U.S. Pat. No. 5,716,981; incorporated herein by reference); AGM-1470 (Ingber et al., 1990; incorporated herein by reference); **shark cartilage extract** (U.S. Pat. No. 5,618,925; incorporated herein by reference); anionic polyamide or polyurea oligomers (U.S. Pat. No. 5,593,664; incorporated herein by. . .

=> d hit

L2 ANSWER 1 OF 1 USPATFULL

DETD Further useful agents include compounds that interfere with DNA replication, mitosis and chromosomal segregation. Such chemotherapeutic compounds include adriamycin, also known as doxorubicin, etoposide, **verapamil**, podophyllotoxin, and the like. Widely used in a clinical setting for the treatment of neoplasms, these compounds are administered through bolus injections intravenously at doses ranging from 25-75 mg/m<sup>2</sup> at 21 day intervals for adriamycin, to 35-50 mg/m<sup>2</sup> for etoposide intravenously or double the intravenous dose orally.

DETD CAI is a small molecular weight synthetic inhibitor of angiogenesis that acts as a **calcium channel blocker** that prevents actin reorganization, endothelial cell migration and spreading on collagen IV. CAI inhibits neovascularization at physiological attainable concentrations and is well tolerated orally by cancer patients. Clinical trials with CAI have yielded disease stabilization in 49% of cancer patients having progressive disease before treatment.

DETD Further specific angiogenesis inhibitors, including, but not limited to, Anti-Invasive Factor, retinoic acids and paclitaxel (U.S. Pat. No. 5,716,981; incorporated herein by reference); AGM-1470 (Ingber et al., 1990; incorporated herein by reference); **shark cartilage extract** (U.S. Pat. No. 5,618,925; incorporated herein by reference); anionic polyamide or polyurea oligomers (U.S. Pat. No. 5,593,664; incorporated herein by reference); oxindole derivatives (U.S. Pat. No. 5,576,330; incorporated herein by reference); estradiol derivatives (U.S. Pat. No. 5,504,074; incorporated herein by reference); and thiazolopyrimidine derivatives (U.S. Pat. No. 5,599,813; incorporated herein by reference) are also contemplated for use as anti-angiogenic compositions for the combined uses of the present invention.

=> d

L2 ANSWER 1 OF 1 USPATFULL

AN 2001:196603 USPATFULL

TI Cancer treatment methods using therapeutic conjugates that bind to aminophospholipids

IN Thorpe, Philip E., Dallas, TX, United States

Ran, Sophia, Dallas, TX, United States

PA Board of Regents, The University of Texas System, Austin, TX, United States (U.S. corporation)

PI US 6312694 B1 20011106

AI US 1999-351457 19990712 (9)

PRAI US 1998-92589 19980713 (60)

US 1998-110600 19981202 (60)

DT Utility  
 FS GRANTED  
 LN.CNT 8243  
 INCL INCLM: 424/178.100  
 INCLS: 424/133.100; 424/134.100; 424/135.100; 424/136.100; 424/137.100;  
 424/141.100; 424/142.100; 424/143.100; 424/181.100; 424/193.100;  
 514/012.000; 530/387.100; 530/388.100  
 NCL NCLM: 424/178.100  
 NCLS: 424/133.100; 424/134.100; 424/135.100; 424/136.100; 424/137.100;  
 424/141.100; 424/142.100; 424/143.100; 424/181.100; 424/193.100;  
 514/012.000; 530/387.100; 530/388.100  
 IC [7]  
 ICM: A61K039-395  
 ICS: C12P021-08; C07K016-00  
 EXF 514/12; 424/133.1; 424/135.1; 424/136.1; 424/137.1; 424/141.1;  
 424/142.1; 424/143.1; 424/178.1; 424/181.1; 424/193.1; 530/387.1;  
 530/388.1  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> s (shark cartilage) and (anti(w)hypertens? or antihypertensive or ((Calcium or  
 Ca) (2w) blocker#) or verapamil or nifedipin or diltiasem)

1189 SHARK  
 351 SHARKS  
 1407 SHARK  
 (SHARK OR SHARKS)  
 6873 CARTILAGE  
 447 CARTILAGES  
 7064 CARTILAGE  
 (CARTILAGE OR CARTILAGES)  
 88 SHARK CARTILAGE  
 (SHARK(W) CARTILAGE)  
 220674 ANTI  
 19 ANTIS  
 220683 ANTI  
 (ANTI OR ANTIS)  
 16378 HYPERTENS?  
 2456 ANTI(W) HYPERTENS?  
 5646 ANTIHYPERTENSIVE  
 1789 ANTIHYPERTENSIVES  
 6689 ANTIHYPERTENSIVE  
 (ANTIHYPERTENSIVE OR ANTIHYPERTENSIVES)  
 215896 CALCIUM  
 54 CALCIUMS  
 215898 CALCIUM  
 (CALCIUM OR CALCIUMS)  
 111832 CA  
 12083 CAS  
 121951 CA  
 (CA OR CAS)  
 10010 BLOCKER#  
 2056 (CALCIUM OR CA) (2W) BLOCKER#  
 1928 VERAPAMIL  
 3 VERAPAMILS  
 1928 VERAPAMIL  
 (VERAPAMIL OR VERAPAMILS)  
 82 NIFEDIPIN  
 2 DILTIASEM  
 L3 2 (SHARK CARTILAGE) AND (ANTI(W) HYPERTENS? OR ANTIHYPERTENSIVE OR  
 ((CALCIUM OR CA) (2W) BLOCKER#) OR VERAPAMIL OR NIFEDIPIN OR  
 DILTIASEM)

=> s 13 not 12  
L4 1 L3 NOT L2

=> d bib,hit

L4 ANSWER 1 OF 1 USPATFULL  
AN 2001:182585 USPATFULL  
TI Compositions and methods for prevention and treatment of chronic diseases and disorders including the complications of diabetes mellitus  
IN Kosbab, John V., Dillon, CO, United States  
PI US 2001031744 A1 20011018  
AI US 2001-827251 A1 20010405 (9)  
RLI Continuation of Ser. No. US 1998-18273, filed on 4 Feb 1998, ABANDONED  
PRAI US 1997-37084 19970204 (60)  
US 1997-43262 19970417 (60)  
DT Utility  
FS APPLICATION  
LREP GREENLEE WINNER and SULLIVAN, P.C., Suite 201, 5370 Manhattan Circle, Boulder, CO, 80303  
CLMN Number of Claims: 32  
ECL Exemplary Claim: 1  
DRWN No Drawings  
LN.CNT 2318  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
SUMM [0024] (iv) A neovascular regulator selected from genistein and/or daidzein; soy isolate comprising genistein and/or daidzein; cartilage or chondroitin sulphate; chondroitin sulphate is a preferred neovascular regulator also associated with collagen synthesis; **shark cartilage** is a preferred cartilage preparation.  
SUMM [0211] A source of cartilage or a cartilage preparation, e.g., **shark cartilage**.  
SUMM [0235] (iii) A neovascular regulator selected from genistein and/or diadzein; soy isolate comprising genistein and/or diadzein; **shark cartilage** or chondroitin sulphate.  
SUMM [0245] Glucosamine sulphate; and optionally a cartilage preparation, e.g., **shark cartilage**  
SUMM [0372] One or more of the functionalities listed in Table 1 can be provided in the compositions of this invention by art-known drug equivalents. For example, art-known antidiabetic agents, **antihypertensives**, angiotensin converting enzyme inhibitors, vasodilators, anticholesteremics, antihyperlipoproteinemics, angiogenesis regulators, and enzyme co-factors can be combined in effective amounts for ameliorating symptoms and conditions associated with microangiopathy, particularly retinopathy and nephropathy, with formulas of this invention.  
SUMM [0406] Green tea extract, tea polyphenols, contains a small amount of 2-3% of proanthocyanidin. It nevertheless is a potent antioxidant for lipid peroxides, superoxides and hydroxyl radicals. It contains relatively high concentrations of (-) epigallocatechin gallate (EGCg), a condensed tannin polyphenol. In addition to antioxidant function, tea polyphenols also have anti-platelet, anti-cholesterolemia, **anti-hypertension**, anti-hyperglycemic and anti-mutagenic activities. Tea polyphenols also assist theoflavin digallate in acting as an angiotensin converting enzyme inhibitor, but do not have the undesired pro-oxidant properties of captopril.  
SUMM [0411] Cartilage, an avascular tissue, is a source of angiogenesis

inhibitor(s). Shark and bovine cartilage, among others, are sources of angiogenesis inhibitor and may provide collagenase inhibition as well. Chondroitin sulphate, a mucopolysaccharide found in most mammalian cartilaginous tissues and **shark cartilage**, is believed by many to be the most active angiogenesis regulating component of **Shark Cartilage**. The restoration of diabetic depleted chondroitin sulphates may also affect collagen stabilization which would help to normalize the collagen matrix of vascular tissue and therefore create a more stable vascular structure. Chondroitin sulphate can be provided in a number of forms with different counterions, e.g., sodium, potassium, etc. Sodium chondroitin sulphate is the form preferred for use in compositions of this invention.

SUMM [0414] Heparin sulphate levels are increased in diabetics while levels of chondroitin sulphates are decreased. This suggests an imbalance in chondroitin sulphate and in angiogenic regulation. Gymnema Sylvestre which normalizes heparin levels is provided in the compositions of this invention, at least in part, to affect heparin levels which in turn may affect angiogenic regulation due to **shark cartilage** and protamine sulfate which both bind to heparin. The insulin/glucose stabilization effects of Gymnema sylvestre would reduce the oxidative stress that contributes to the neovascularization factors described above.

SUMM [0457] Gymnemic acid, the active ingredient in Gymnema sylvestre, suppresses sensitivity to sugar and its absorption, thereby reducing blood glucose levels. It also restores the levels of three chondroitin sulfates which may assist in collagen repair and/or aid in angiogenesis regulation. Heparin sulphate levels are increased in diabetics while three chondroitin sulfates are decreased. Gymnema sylvestre which normalizes heparin levels could play a supporting role in the angiogenic regulation of other ingredients in this formulation, namely **shark cartilage** and protamine sulfate. Both are angiogenic regulators which bind to heparin. The restoration of depleted chondroitin sulfates probably plays a role in collagen stabilization which would help to normalize the collagen matrix and therefore create a more stable structure upon which angiogenesis regulation could more easily exist. The insulin/glucose stabilization effects of Gymnema sylvestre would reduce the oxidative stress that contributes to the neovascularization factors described above.

DETD [0496] **Shark cartilage** powder (100%, 200 mesh) was obtained from Global Trading (USA) Inc. (Union, N.J.).

DETD [0503] Those of ordinary skill in the art of formulation of nutrients and therapeutic compositions will appreciate that components functionally equivalent to those specifically disclosed herein, as well as alternative forms and sources in addition to those specifically disclosed herein for individual composition ingredients are available. This invention is intended to encompass all such functional equivalents and alternatives that are readily known to the art.

#### TABLE 1

Summary of Functions of Components of Compositions of this invention for Microangiopathy and Macroangiopathy

Primary formulas comprise components which:

1. Function as antioxidant to control oxidative stress;
2. Function as neovascular regulators controlling angiogenesis to promote vascular healing and integrity;
3. Stabilize glucose and amylase factors, for example, to increase

- glucose tolerance in diabetes; and
4. Supplement dietary deficiencies and loss through spillage, particularly as associated with diabetes.
- Compositions of this invention can further comprise components which:
5. Stabilize insulin supply and decrease sensitivity to glucose;
  6. Stabilize protein factors, control proteinuria, glycosylation and albumin;
  7. Control anti-sclerotic factors, functioning as/to:
    - A. Anti-platelet or anti-thrombic agents
    - B. Homocysteine inhibitors
    - C. Reduce atherosclerotic lesions
    - D. Reduce LDL and VLDL
    - E. Improve HDL/LDL ratio
    - F. Inhibit lipoprotein (a) production
    - G. Inhibit cholesterol absorption in bowel
    - H. Enhance cholesterol excretion
    - I. Triglycerides inhibitors
    - J. Fibrogen inhibitors
    - K. Nitric Oxide inhibitors (Optional)
    - L. Ketosis regulators
  8. Reduce immune phagocytic response to:
    - A. Leukotrienes, neutrophils, etc.
    - B. Immunoglobulin (a)
  9. Reduce and stabilize **anti-hypertensives** as:
    - A. Angiotensin converting enzyme inhibitors & vasodilators
    - B. Prostacyclin inhibitors
    - C. Aldose Reductase inhibitors
    - D. Blood pressure inhibitor/regulator (systolic only)
    - E. Agents to reduce blood pressure during bowel contractions
    - F. Anti-edema agent
    - G. Histamine suppressors
  10. Enhance cellular or metabolic function, for example for:
    - A. Glutathione restoration
    - B. ATP/NAD restoration
  11. Promote vascular healing and integrity by:
    - A. Restoring the collagen matrix
    - B. Histamine suppression (Optional)
  12. Promote better nutrient digestion and absorption
  13. Improve pH factor by controlling digistens and systemic hyperacidity
  14. Participate in collagen synthesis
  15. Calcium regulator
  16. Control myocardial infarction and damage
  17. Increase cardiovascular exercise ability and tolerance
  18. Increase other antioxidants, including Vitamin E, reduced glutathione, uric acid, superoxide dismutase (SOD), catalyze, or glutathione peroxidase
  19. Inhibit breakdown of myocardial cell membrane
  20. Provide immune differentiation
  21. Restore Vitamin E levels by intestinal absorption of omega-3-fatty acids
  22. Improves cell transport and mitochondrial function
  23. Improves sleep for better disease resistance and recovery
  24. Amino acid believed to inhibit or ameliorate diabetes pathogenesis
  25. Amino acid believed to inhibit or ameliorate cardiovascular pathogenesis
  26. Amino acid believed to contribute to wound healing or prevention
  27. Amino acid believed to inhibit or ameliorate neuropathic pathogenesis
  28. Amino acid believed to inhibit or ameliorate dental and periodontal pathogenesis
  29. Promoter of DNA polymerase for wound healing
  30. Provides protein sources for wound healing
  31. Contributes to improved bone density

32. Promotes anti-caries and anti-gingivitis environment

33. Accelerates wound healing

DETD [0506]

TABLE 4

Exemplary Diabetic Compliations Formulation Dosages

COMPONENT	AVERAGE ADULT DOSE PER DAY - mg/day FORMULATION A	AVERAGE ADULT DOSE PER DAY - mg/day FORMULATION B
Bilberry Extract, 25% OPC	375	375
Calcium (Krebs)	500 (110 active)	500 (110 active)
Chondroitin Sulfate	750	750
Chromium Picolinate	200 .mu.g (24.60 .mu.g active)	200 .mu.g (24.60 .mu.g active)
CoQ10	20	20
Fenugreek Seed Powder	150	150
Flax Seed Powder	500	500
Folic Acid	800 .mu.g	450 .mu.g
Linoleic Acid	25	25
Ginko Biloba 24%	25	25
Gymnema Sylvestre	250	250
Taurine or Homotaurine	100	100
Grape Seed extract, 95-100% OPC	100	100
Acetyl-l-carnitine	50	50
Lutein	120	120
Magnesium (Krebs)	300 (48 active)	300 (48 active)
N-Acetyl-l-cysteine	200	200
Pine Bark Extract (greater than 85% OPC)	20	20
Phytosterol Complex (Cholestatin III)	200	200
Potassium Citrate	90 (32.4)	90 (32.4)
Protamine Sulfate	50	50
<b>Shark Cartilage</b> 100%	1,000	1,000
Soy Isolate	1,000 (920 active)	1,000 (920 active)
Green Tea Polyphenols	100	100
Lipoic Acid	20	20
Vitamin A (Acetate Formula A) (Palmitate Formula B)	5,000 iu	5,000 iu
Vitamin B-2 (Riboflavin)	3	50
Vitamin B-6 (Pyridoxine hydro- chloride)	4.88 active (4.0 active)	213.4 (175 active)
Vitamin B-12 (Cyanocobalamin 1%)	100 .mu.g active	100 .mu.g active
Vitamin C (Ascorbic acid)	1,000	1,000
Vitamin E, d-alpha tocopheryl acetate	714 (500 iu active)	714 (500 iu active)
Zinc (Krebs)	30 (9 active)	30 (9 active)

=> file caplus  
COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
42.22	44.02

FULL ESTIMATED COST

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FILE COVERS 1907 - 9 Jan 2002 VOL 136 ISS 2  
FILE LAST UPDATED: 7 Jan 2002 (20020107/ED)

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FILE 'USPATFULL' ENTERED AT 13:40:16 ON 09 JAN 2002

L1	5 S ((SHARK CARTILAGE) (2A) EXTRACT)/CLM
L2	1 S ((SHARK CARTILAGE) (2A) EXTRACT) AND (ANTI(W)HYPERTENS? OR AN
L3	2 S (SHARK CARTILAGE) AND (ANTI(W)HYPERTENS? OR ANTIHYPERTENSIVE
L4	1 S L3 NOT L2

FILE 'CAPLUS' ENTERED AT 13:54:01 ON 09 JAN 2002

=> s 12

3041 SHARK  
832 SHARKS  
3338 SHARK  
(SHARK OR SHARKS)

17498 CARTILAGE  
 824 CARTILAGES  
 17628 CARTILAGE  
 (CARTILAGE OR CARTILAGES)  
 170 SHARK CARTILAGE  
 (SHARK(W) CARTILAGE)  
 21958 EXTRACT  
 28628 EXTRACTS  
 49577 EXTRACT  
 (EXTRACT OR EXTRACTS)  
 252469 EXT  
 188279 EXTs  
 397312 EXT  
 (EXT OR EXTs)  
 410797 EXTRACT  
 (EXTRACT OR EXT)  
 20 (SHARK CARTILAGE) (2A) EXTRACT  
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 7 ANTIS  
 261327 ANTI  
 (ANTI OR ANTIS)  
 62745 HYPERTENS?  
 396 ANTI(W) HYPERTENS?  
 21019 ANTIHYPERTENSIVE  
 20808 ANTIHYPERTENSIVES  
 26999 ANTIHYPERTENSIVE  
 (ANTIHYPERTENSIVE OR ANTIHYPERTENSIVES)  
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 8780 (CALCIUM OR CA) (2W) BLOCKER#  
 14525 VERAPAMIL  
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 14526 VERAPAMIL  
 (VERAPAMIL OR VERAPAMILS)  
 31 NIFEDIPIN  
 1 DILTIASEM  
 L5 1 ((SHARK CARTILAGE) (2A) EXTRACT) AND (ANTI(W) HYPERTENS? OR ANTIH  
 YPERTENSIVE OR ((CALCIUM OR CA) (2W) BLOCKER#) OR VERAPAMIL OR  
 NIFEDIPIN OR DILTIASEM)

=> d bib,kwic

L5 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS  
 AN 1999:64822 CAPLUS  
 DN 130:90515  
 TI A preparation derived from shark cartilage for treatment of diseases  
 related to excessive parathyroid hypertensive factor or excessive  
 intracellular calcium  
 IN Pang, Peter K. T.; Shan, Jacqueline J.; Chiu, Kam W.  
 PA CV Technologies Inc., Can.  
 SO PCT Int. Appl., 30 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1



	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9902548	A1	19990121	WO 1998-US13591	19980709
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9883790	A1	19990208	AU 1998-83790	19980709
	EP 1012163	A1	20000628	EP 1998-934212	19980709
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	JP 2001509513	T2	20010724	JP 2000-502067	19980709
PRAI	US 1997-52233	P	19970711		
	WO 1998-US13591	W	19980709		

RE.CNT 6

RE

- (1) Dupont; US 5618925 A 1997 CAPLUS
- (2) Furuhashi; US 3371012 A 1968
- (3) Lane; US 5075112 A 1991
- (4) Pang; US 5192664 A 1993 CAPLUS
- (6) Schinitzky; US 4473551 A 1984 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB **Shark cartilage ext.** has been shown to be an antagonist of parathyroid hypertensive factor (PHF). In view of this, **shark cartilage ext.** can be used to treat conditions related to excessive PHF activity. Such diseases include hypertension and some other diseases related to intracellular calcium elevation. Methods for producing the **shark cartilage ext.** and methods for administering the ext. are disclosed.

ST **shark cartilage ext** parathyroid hypertensive factor inhibition hypotensive; calcium disease **shark cartilage ext** parathyroid hypertensive factor inhibition

IT Mucopolysaccharides, biological studies  
 Proteins (general), biological studies  
 RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)  
 (in **shark cartilage ext.**; **shark cartilage ext.** for treatment of diseases related to excessive parathyroid hypertensive factor or excessive intracellular calcium)

IT Vascular smooth muscle  
 (proliferation inhibition; **shark cartilage ext.** for treatment of diseases related to excessive parathyroid hypertensive factor or excessive intracellular calcium)

IT **Antihypertensives**  
 Cartilage  
 Drug delivery systems  
 Shark  
 (shark cartilage ext. for treatment of diseases related to excessive parathyroid hypertensive factor or excessive intracellular calcium)

IT Antiproliferative agents  
 (vascular smooth muscle; **shark cartilage ext.** for treatment of diseases related to excessive parathyroid hypertensive factor or excessive intracellular calcium)

IT 25322-46-7, Chondroitin sulfate C  
 RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)  
 (in **shark cartilage ext.**; **shark**

**cartilage ext.** for treatment of diseases related to excessive parathyroid hypertensive factor or excessive intracellular calcium)

IT 7440-70-2, Calcium, biological studies 130037-95-5, Parathyroid hypertensive factor  
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)  
(**shark cartilage ext.** for treatment of diseases related to excessive parathyroid hypertensive factor or excessive intracellular calcium)

=> file wpids

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	22.49	66.51
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.62	-0.62

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FILE LAST UPDATED: 05 JAN 2002 <20020105/UP>  
MOST RECENT DERWENT UPDATE 200201 <200201/DW>  
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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=> s 12

431 SHARK  
82 SHARKS  
462 SHARK  
(SHARK OR SHARKS)  
2352 CARTILAGE  
96 CARTILAGES  
2399 CARTILAGE  
(CARTILAGE OR CARTILAGES)  
43 SHARK CARTILAGE  
(SHARK(W) CARTILAGE)  
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147828 EXTRACT  
(EXTRACT OR EXTRACTS)  
1075 EXT  
93 EXT  
1128 EXT  
(EXT OR EXT)  
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(EXTRACT OR EXT)  
11 (SHARK CARTILAGE) (2A) EXTRACT  
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9 ANTIS

151100 ANTI  
 (ANTI OR ANTIS)  
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 789 ANTI (W) HYPERTENS?  
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 93840 CALCIUM  
 (CALCIUM OR CALCIUMS)  
 168149 CA  
 1267 CAS  
 169233 CA  
 (CA OR CAS)  
 3593 BLOCKER#  
 521 (CALCIUM OR CA) (2W) BLOCKER#  
 384 VERAPAMIL  
 1 VERAPAMILS  
 384 VERAPAMIL  
 (VERAPAMIL OR VERAPAMILS)  
 51 NIFEDIPIN  
 1 DILTIASEM  
 L6 1 ((SHARK CARTILAGE) (2A) EXTRACT) AND (ANTI(W)HYPERTENS? OR ANTIH  
 YPERTENSIVE OR ((CALCIUM OR CA) (2W) BLOCKER#) OR VERAPAMIL OR  
 NIFEDIPIN OR DILTIASEM)

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L6 ANSWER 1 OF 1 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD  
 AN 1999-120772 [10] WPIDS  
 DNC C1999-035371  
 TI **Shark cartilage extract** - has  
 anti-parathyroid hypertensive factor activity.  
 DC B04  
 IN CHIU, K W; PANG, P K T; SHAN, J J  
 PA (CVTE-N) CV TECHNOLOGIES INC  
 CYC 83  
 PI WO 9902548 A1 19990121 (199910)\* EN 29p C07K001-00  
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 OA PT SD SE SZ UG ZW  
 W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE  
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 MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG  
 US UZ VN YU ZW  
 AU 9883790 A 19990208 (199924) C07K001-00  
 EP 1012163 A1 20000628 (200035) EN C07K001-00  
 R: AT CH DE FI FR GB LI  
 CN 1263534 A 20000816 (200055) C07K001-00  
 JP 2001509513 W 20010724 (200147) 32p A61K035-32  
 KR 2001021764 A 20010315 (200159) C07K001-00  
 ADT WO 9902548 A1 WO 1998-US13591 19980709; AU 9883790 A AU 1998-83790  
 19980709; EP 1012163 A1 EP 1998-934212 19980709; WO 1998-US13591 19980709;  
 CN 1263534 A CN 1998-807088 19980709; JP 2001509513 W WO 1998-US13591  
 19980709; JP 2000-502067 19980709; KR 2001021764 A KR 2000-700327 20000111  
 FDT AU 9883790 A Based on WO 9902548; EP 1012163 A1 Based on WO 9902548; JP  
 2001509513 W Based on WO 9902548  
 PRAI US 1997-52233P 19970711  
 IC ICM A61K035-32; C07K001-00  
 ICS A61K031-715; A61K038-00; A61P003-10; A61P009-00; A61P009-12;  
 A61P043-00; C07K001-02